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EXAMINER	
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1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,856	LAUS ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *06 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1 and 23-26* is/are pending in the application.

4a) Of the above claim(s) *23-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: *Appendix 1 and Appendix 2.* Appendix 3

1. The Election filed October 6, 2006 in response to the Office Action of September 6, 2006 is acknowledged and has been entered. Claims 1 and 23-26 are pending in the application and Claims 23-26 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claim 1 is currently under prosecution.

2. Applicant's election with traverse of Group 1, claim 1 is acknowledged. The traversal is on the ground(s) that examination of all groups would not impose a serious burden on the examiner because the method of Group II makes use of the polypeptide of Group I, particularly in view of searches previously made in US Patent Application No. 09/402,845. In particular, an updated search is not required because the priority date remains the same. This is not found persuasive because the priority date in fact does not remain the same. As set forth below, claim 1, as originally filed in this application and as currently constituted, is not drawn to the subject matter of the '845 application because the '845 application is drawn to isolated polypeptide comprising 90% identity to SEQ ID NO:2, antibodies thereto and methods of making said antibodies. The subject matter of claim 1 as originally filed in this application is drawn to a polypeptide that is immunoreactive with an antibody that is immunoreactive with human PAP comprising an amino acid sequence represented as SEQ ID NO:2, including conservative amino acid substitutions that do not alter the sequence by more than 10%. Thus, the claim as originally filed is not drawn to a polypeptide with 90% identity to SEQ NO:2, but rather is drawn to a polypeptide with an identity of only a single epitope that will cross react with antibody that cross reacts with SEQ ID NO:2 or a conservatively substituted SEQ ID NO:2. Given that the art recognizes that only five or six amino acids will form an epitope, given that SEQ ID NO:2 is 385 amino acids in length,

the claim as originally filed in this case is in fact drawn to an isolated polypeptide with 1% identity to SEQ ID NO:2. This polypeptide is neither taught nor contemplated in the '845 application and therefore this invention does not have the priority date of the prior application. Thus, updated search is required because different searches and issues are involved with the examination of the instantly claimed invention when compared to the invention of the '845 patent application. Further, as drawn to the instantly claimed inventions, the literature search, particularly relevant in this field although overlapping, is not coextensive. Different searches and issues are involved with the examination of each group. Applicant further argues that in the restriction of US Patent Application No. 09/402,845, both polypeptide and methods of inducing an immune response with said polypeptide were found to have unity of invention and therefore the instantly claimed inventions have unity of invention. The argument has been considered but has not been found persuasive because the prior application was filed under 35 USC 371 and thus restriction practice appropriate to that filing was followed. However, the instant case is not a national filing of an international application and therefore is not accorded 35 USC 371 practice. For these reasons the restriction requirement is deemed to be proper and made Final.

Is noted for Applicant's convenience that as previously set forth, should claim 1 become allowable, the invention of Group II will be rejoined to the invention of Group I and examined, as per Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

3. It is noted that a priority date of February 4, 2004 has been established for the instant invention because a review of the specification of US Patent

Application No. 09/402,845 did not reveal support for the originally filed claim 1 drawn to an isolated polypeptide which is immunoreactive with an antibody that is itself immunoreactive with human prostate acid phosphatase comprising an amino acid sequence presented as SEQ ID NO:2 including conservative amino acid substitutions that do not alter the sequence by more than 10%. A review of the prior specification revealed support for SEQ ID NO:2, for SEQ ID NO:2 including conservative amino acid substitutions that do not alter the sequence by more than 10%, but not for an isolated polypeptide that is immunoreactive with an antibody that is itself immunoreactive with PAP. If Applicant disagrees with any rejections based on the establishment of February 4, 2004 as the priority date of the instant Application, Applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Objections

4. The claims as filed in the original specification are part of the disclosure and therefore, if an application as originally filed contains a claim disclosing material not disclosed in the remainder of the specification, the applicant may amend the specification to include the claimed subject matter. In re Benno, 768 F.2d 1340, 226 USPQ 683 (Fed. Cir. 1985).The specification is objected to as failing to provide proper antecedent basis for the subject matter of claim 1, that is the specification does not provide antecedent basis for an isolated polypeptide which is immunoreactive with an antibody that is itself immunoreactive with human prostatic acid phosphatase (PAP) comprising (a) an amino acid sequence presented as SEQ ID NO: 2, including conservative amino acid substitutions that do not alter the sequence by more than 10%, as originally filed. Appropriate correction is required. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 1 is rejected under 35 USC 101 because the disclosed invention is inoperative and therefore lacks utility.

The claims are drawn to an isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from (a) an amino acid sequence of SEQ ID NO:2 and (b) a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2.

The claim is inoperative because a review of the information in the specification reveals that SEQ ID NO:2 is a murine and not a human polypeptide, further a review of the literature does not reveal a single instance wherein a human PAP has 90% identity to SEQ ID NO:2 (see attached Appendix 1).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising SEQ ID

NO:2, does not reasonably provide enablement for an isolated polypeptide that is immunoreactive with an antibody that is also immunreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to an isolated polypeptide that is immunoreactive with an antibody that is also immunreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2. This means that the claims are drawn to a polypeptide with an identity of as little as a single epitope that will cross react with antibody that cross reacts with SEQ ID NO:2 or a conservatively substituted SEQ ID NO:2. Given that the art recognizes that only five or six amino acids will form an epitope, given that SEQ ID NO:2 is 385 amino acids in length, the claim as originally filed in this case is in fact drawn to an isolated polypeptide with as little as 1% identity to SEQ ID NO:2.

The specification teaches that the invention includes a novel tumor-related antigen, mouse prostatic acid phosphatase (mPAP) which can be used as a xenogeneic antigen to induce prostate-directed immunity in other mammalian species (p. 2, lines 12-15), SEQ ID NO:2 and further teaches that the invention includes isolated polypeptides that have about 90%, and preferably at least 95% sequence identity to the sequence presented as SEQ ID NO: 2 (mPAP). It is further appreciated that the PAP antigen can be formed by substituting into the polypeptide sequence identified as SEQ ID N0: 2, amino acids that represent

conservative substitutions according to the teachings presented herein. Preferably, such conservative substitutions will not alter the mPAP sequence by more than about 10% (p. 2, lines 25-31).

One cannot extrapolate the teaching of the specification to the scope of the claims because it would not be expected, nor would it be predicted that the instantly claimed polypeptide would be useful as a xenogeneic antigen to induce prostate-directed immunity in any species as contemplated in the specification given that the claimed polypeptide is drawn to polypeptides with as little as five amino acids in common with SEQ ID NO:2. Further, although SEQ ID NO:2 is known to be a PAP and one would know how to use the PAP, not only as an immunogen but also as a phosphatase, the instantly claimed polypeptide is drawn to a polypeptide comprising as little as 1% identity with SEQ ID NO:2 and those of ordinary skill in the art recognize the unpredictability of the protein chemistry arts. In particular, applicant has not shown that the claimed polypeptides are capable of functioning as that which is being disclosed. Applicant has not enabled all of these types of modified polypeptides because it is well known in the art that the effects, on the functionality of a polypeptide, of altering even one amino acid cannot be predicted. For example, Bowie et a1, (Science, 1990,247:1306-1310, IDS item) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino

acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 1 1 1 :2 129-2 13 8,1990) who teach that replacement of a single lysine reside at position 11 8 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et a1 (Molecular and Cellular Biology, 1988, 8:1247-1252. IDS item) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagme did not affect biological activity while replacement with serine or glutarnic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly with up to 99% difference between SEQ ID NO:2 and the claimed polypeptides it could not be predicted, nor would it be expected that the function and activity of the claimed polypeptides would be the same as that of SEQ ID NO:2 and if it did not have the same activity as SEQ ID NO:2, one would not know how to use the claimed invention. Further, as drawn to the contemplated function of producing a prostate specific immune response, given the clear teaching of Bowie et al that the amino acid sequence encodes a message that determines the shape of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, it is clear

that it cannot be predicted that the claimed polypeptides with as little as 1% identity to SEQ ID NO:2 could fold into a three dimensional structure that would permit the production of a prostate specific immune response because it cannot be predicted, for example, whether or not an epitope shared with SEQ ID NO:2 would be even displayed on the surface of the molecule so that it would be accessible to cells of the immune system. Indeed, if the claimed polypeptide could not produce a prostate specific immune response, one would not know how to use the claimed invention.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the polypeptide would function as contemplated with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

8. Claim 1 is rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 1 is drawn to an isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2. The specification teaches the invention includes a novel tumor-related antigen, mouse prostatic acid phosphatase (mPAP) which can be used as a xenogeneic antigen to induce prostate-directed immunity in other mammalian species (p. 2, lines 12-15), SEQ ID NO:2 and further teaches that the invention includes isolated polypeptides that have about 90%, and preferably at least 95%

sequence identity to the sequence presented as SEQ ID NO: 2 (mPAP). It is further appreciated that the PAP antigen can be formed by substituting into the polypeptide sequence identified as SEQ ID N0: 2, amino acids that represent conservative substitutions according to the teachings presented herein. Preferably, such conservative substitutions will not alter the mPAP sequence by more than about 10% (p. 2, lines 25-31). It is noted that the claim as currently constituted is not drawn to the polypeptides taught in the specification, but rather is drawn to a polypeptide with an identity of as little as a single epitope that will cross react with antibody that cross reacts with SEQ ID NO:2 or a conservatively substituted SEQ ID NO:2. Given that the art recognizes that only five or six amino acids will form an epitope, given that SEQ ID NO:2 is 385 amino acids in length, the claim as originally filed in this case is in fact drawn to an isolated polypeptide with as little as 1% identity to SEQ ID NO:2.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by

> function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description of the claimed isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2, per Lilly by structurally describing a representative number of the claimed isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the claimed isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any isolated polypeptide that is immunoreactive with an antibody that

is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 other than SEQ ID NO:2, nor does the specification provide any partial structure of such isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2, nor any physical or chemical characteristics of the claimed isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 nor any functional characteristics coupled with a known or disclosed correlation between structure and function, other than SEQ ID NO:2. Although the specification discloses SEQ ID NO:2, this does not provide a description of the claimed isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 that would satisfy the standard set out in Enzo.

The specification also fails to describe the claimed isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 by the test set out in Lilly. The specification

describes only a single isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2

Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the claimed isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 that is required to practice the claimed invention and does not meet the written description requirements of 35 USC 112, first paragraph.

9. Claim 1 is rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of an isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2 claimed in 1 has no clear support in the specification and the claims as originally filed. A review of the instant specification reveals support for "The isolated PAP polypeptide has at least about 90% , and preferably at least 95% sequence identity to **the** (emphasis

added) sequence presented as SEQ ID NO: 2 (mPAP). It is further appreciated that the PAP antigen can be formed with by substituting into the polypeptide sequence identified as SEQ ID N0: 2 amino acids that represent conservative substitutions according to the teachings presented herein. Preferably, such conservative substitutions will not alter the mPAP sequence by more than about 10% ." However, nothing in the specification appears to be drawn to an isolated polypeptide that is immunoreactive with an antibody that is immunoreactive with human PAP, "an amino acid sequence of SEQ ID NO:2", "a variant having at least 90% identity to an amino acid sequence of SEQ ID NO:2" which in point of fact reads a variant comprising as little as 5 amino acids of SEQ ID NO:2 which is generally considered the smallest number of amino acids required for an antibody epitope. The instantly claim is clearly drawn to a polypeptide that varies more than 10% from SEQ ID NO:2. The subject matter claimed in claim 1 broadens the scope of the invention as originally disclosed in the specification. Applicant is invited to point to page and line of the instant application wherein support for the newly added amendments may be found.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claims 1 is rejected under 35 U.S.C. § 102(e) as being anticipated by US Patent No. 5,882,864 as evidenced by Roitt et al, (Immunology, 1993, Mosby, St. Louis, p 6.4-6.5) and Bost et al. (Immunol. Invest. 1988; 17:577-586).

Claim 1 is drawn to an isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2.

Roitt et al (Immunology, 1993, Mosby, St. Louis, p 6.4-6.5).teach that when the determinants of antigen A are shared by another antigen, B, then antibodies that bind to those determinants in A will also react with B. This phenomenon is termed cross-reactivity (see Fig 6.8 on page 6.4 and p. 6.5, para 1). This is exemplified by Bost et al who teach antibodies which "cross-react" with IL-2 and HIV envelope protein and establishes that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4 of 6 residues were identical (see entire document, but especially the Abstract and Discussion). Thus, antibody that "binds specifically" to a specific epitope will also bind specifically to other proteins that share the same epitope. Examiner takes note that those of ordinary skill in the art recognize that a grouping of the order of about four or five amino acids, contiguous or not, is regarded as a typical number of amino acids in a minimal epitope.

It is assumed for examination purposes that "an amino acid sequence of SEQ ID NO:2" refers to any subsequence of SEQ ID NO:2 of at least four or five amino acids and that a "variant having at least 90% identity to the amino acid sequence of

an amino acid sequence of SEQ ID NO:2 refers to any subsequence of SEQ ID NO:2 of ten amino acids wherein at least 9 of those amino acids are identical to SEQ ID NO:2.

US Patent No. 5,882,864 teaches an isolated antibody that binds to SEQ ID NO:48, wherein SEQ ID NO:48 is 80% identical to SEQ ID NO:2 (see appendix 3 comparison) and has numerous stretchs of "100% identity with an amino acid sequence of SEQ ID NO:2" identity to SEQ ID NO:2 or a variant thereof comprising 9 or more amino acids identical to SEQ ID NO:2. Given that the identity between SEQ ID NO:48 and SEQ ID NO:2, it would be expected that at least a subset of the antibodies that bind to SEQ ID NO:48 would also cross react and therefore bind to an amino acid sequence of SEQ ID NO:2. Although the reference does not specifically teach that the prior art polypeptide is immunoreactive with an antibody that is also immunoreactive with an amino acid sequence of SEQ ID NO:2, given the 80.7 percent identity of the two polypeptides, the claimed polypeptide appears to be the same as the prior art polypeptide, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

13. Claims 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Sharief et al (Biochem. Biophys. Res. Commun.) 184:1468-1476(1992).

Claim 1 is drawn to an isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2.

Sharief et al teach human PAP (see Attached Appendix 2). Given that the isolated polypeptide of Sharief et al is human PAP, it is an inherent property of the isolated polypeptide to immunoreact with an antibody that is immunoreactive with itself. All of the limitations of the claim are met.

14. Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Sharief et al (Biochem. Biophys. Res. Commun.) 184:1468-1476(1992) as evidenced by Roitt et al, Supra, and Bost et al. Supra.

Claim 1 is drawn to an isolated polypeptide that is immunoreactive with an antibody that is also immunoreactive with human prostatic acid phosphatase selected from an amino acid sequence of SEQ ID NO:2 and a variant having at least 90% identity to the amino acid sequence of an amino acid sequence of SEQ ID NO:2.

Roitt et al, Supra and Bost et al, Supra teach as set forth above.

Sharief et al teach human PAP with 80.7% identity to SEQ ID NO:2 (see Attached Appendix 2) wherein the polypeptide has numerous stretchs of "100% identity with an amino acid sequence of SEQ ID NO:2" identity to SEQ ID NO:2 or a variant thereof comprising 9 or more amino acids identical to SEQ ID NO:2. Given that the identity between the prior art sequence and SEQ ID NO:2, it would be expected that at least a subset of the antibodies that bind to the prior art sequence would also cross react and therefore bind to an amino acid sequence of

SEQ ID NO:2. Although the reference does not specifically teach that the prior art polypeptide is immunoreactive with an antibody that is also immunoreactive with an amino acid sequence of SEQ ID NO:2, the claimed polypeptide appears to be the same as the prior art polypeptide, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

15. No claims allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898.. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
December 15, 2006

Appendix 2
p. 1

```
<!--StartFragment-->RESULT 5
PPAP_HUMAN
ID   PPAP_HUMAN     STANDARD;      PRT;   386 AA.
AC   P15309;
DT   01-APR-1990, integrated into UniProtKB/Swiss-Prot.
DT   01-MAR-1992, sequence version 3.
DT   07-MAR-2006, entry version 58.
DE   Prostatic acid phosphatase precursor (EC 3.1.3.2).
GN   Name=ACPP;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC   Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RX   MEDLINE=92272747; PubMed=1375464;
RA   Sharief F.S., Li S.S.-L.;
RT   "Structure of human prostatic acid phosphatase gene.";
RL   Biochem. Biophys. Res. Commun. 184:1468-1476(1992).
RN   [2]
RP   NUCLEOTIDE SEQUENCE, PARTIAL PROTEIN SEQUENCE, DISULFIDE BONDS, AND
RP   ACTIVE SITE.
RX   MEDLINE=91115848; PubMed=1989985;
RA   van Etten R.L., Davidson R., Stevis P.E., Macarthur H., Moore D.L.;
RT   "Covalent structure, disulfide bonding, and identification of reactive
RT   surface and active site residues of human prostatic acid
RT   phosphatase.";
RL   J. Biol. Chem. 266:2313-2319(1991).
RN   [3]
RP   NUCLEOTIDE SEQUENCE.
RX   MEDLINE=89228054; PubMed=2712834;
RA   Sharief F.S., Lee H., Leuderman M.M., Lundwall A., Deaven L.L.,
RA   Lee C.-L., Li S.S.-L.;
RT   "Human prostatic acid phosphatase: cDNA cloning, gene mapping and
RT   protein sequence homology with lysosomal acid phosphatase.";
RL   Biochem. Biophys. Res. Commun. 160:79-86(1989).
RN   [4]
RP   NUCLEOTIDE SEQUENCE, AND PARTIAL PROTEIN SEQUENCE.
RC   TISSUE=Prostate;
RX   MEDLINE=88312981; PubMed=2842184; DOI=10.1016/0014-5793(88)80037-1;
RA   Vihko P., Virkkunen P., Henttu P., Roiko K., Solin T., Huhtala M.L.;
RT   "Molecular cloning and sequence analysis of cDNA encoding human
RT   prostatic acid phosphatase.";
RL   FEBS Lett. 236:275-281(1988).
RN   [5]
RP   NUCLEOTIDE SEQUENCE.
RC   TISSUE=Prostate;
RX   MEDLINE=90370491; PubMed=2395659;
RA   Tailor P.G., Govindan M.V., Patel P.C.;
RT   "Nucleotide sequence of human prostatic acid phosphatase determined
RT   from a full-length cDNA clone.";
RL   Nucleic Acids Res. 18:4928-4928(1990).
RN   [6]
RP   NUCLEOTIDE SEQUENCE.
RX   MEDLINE=95038536; PubMed=7951074;
RA   Sharief F.S., Li S.S.-L.;
RT   "Nucleotide sequence of human prostatic acid phosphatase ACPP gene,
RT   including seven Alu repeats.";
RL   Biochem. Mol. Biol. Int. 33:561-565(1994).
RN   [7]
RP   X-RAY CRYSTALLOGRAPHY (2.9 ANGSTROMS).
RX   MEDLINE=99023966; PubMed=9804805; DOI=10.1074/jbc.273.46.30406;
RA   Lacount M.W., Handy G., Lebioda L.;
RT   "Structural origins of L(+)-tartrate inhibition of human prostatic
RT   acid phosphatase.";
RL   J. Biol. Chem. 273:30406-30409(1998).
CC   -!- CATALYTIC ACTIVITY: A phosphate monoester + H(2)O = an alcohol +
CC       phosphate.
CC   -!- SUBUNIT: Homodimer.
CC   -!- SIMILARITY: Belongs to the histidine acid phosphatase family.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; M97589; AAA60021.1; -; Genomic_DNA.
```

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```
DR   EMBL; M97580; AAA60021.1; JOINED; Genomic_DNA.
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DR   EMBL; M97582; AAA60021.1; JOINED; Genomic_DNA.
DR   EMBL; M97583; AAA60021.1; JOINED; Genomic_DNA.
DR   EMBL; M97584; AAA60021.1; JOINED; Genomic_DNA.
DR   EMBL; M97585; AAA60021.1; JOINED; Genomic_DNA.
DR   EMBL; M97586; AAA60021.1; JOINED; Genomic_DNA.
DR   EMBL; M97587; AAA60021.1; JOINED; Genomic_DNA.
DR   EMBL; M97588; AAA60021.1; JOINED; Genomic_DNA.
DR   EMBL; M34840; AAA69694.1; -; mRNA.
DR   EMBL; M24902; AAA60022.1; -; mRNA.
DR   EMBL; X52174; CAA36422.1; -; mRNA.
DR   EMBL; X53605; CAA37673.1; -; mRNA.
DR   EMBL; U07097; AAB60640.1; -; Genomic_DNA.
DR   EMBL; U07083; AAB60640.1; JOINED; Genomic_DNA.
DR   EMBL; U07085; AAB60640.1; JOINED; Genomic_DNA.
DR   EMBL; U07086; AAB60640.1; JOINED; Genomic_DNA.
DR   EMBL; U07088; AAB60640.1; JOINED; Genomic_DNA.
DR   EMBL; U07091; AAB60640.1; JOINED; Genomic_DNA.
DR   EMBL; U07092; AAB60640.1; JOINED; Genomic_DNA.
DR   EMBL; U07093; AAB60640.1; JOINED; Genomic_DNA.
DR   EMBL; U07095; AAB60640.1; JOINED; Genomic_DNA.
DR   PIR; JH0610; JH0610.
DR   PDB; 1CVI; X-ray; A/B/C/D=33-374.
DR   PDB; 1ND5; X-ray; A/B/C/D=33-386.
DR   PDB; 1ND6; X-ray; A/B/C/D=33-386.
DR   PDB; 2HPA; X-ray; A/B/C/D=33-374.
DR   Ensembl; ENSG00000014257; Homo sapiens.
DR   H-InvDB; HIX0022603; -.
DR   HGNC; HGNC:125; ACPP.
DR   MIM; 171790; gene.
DR   GO; GO:0000074; P:regulation of progression through cell cycle; TAS.
DR   InterPro; IPR000560; HisAc_phsphtse.
DR   Pfam; PF00328; Acid_phosphat_A; 1.
DR   PROSITE; PS00616; HIS_ACID_PHOSPHAT_1; 1.
DR   PROSITE; PS00778; HIS_ACID_PHOSPHAT_2; 1.
KW   3D-structure; Direct protein sequencing; Glycoprotein; Hydrolase;
KW   Signal.
FT   SIGNAL        1     32
FT   CHAIN        33    386       Prostatic acid phosphatase.
FT                                 /FTId=PRO_0000023963.
FT   ACT_SITE     44     44       Nucleophile (By similarity).
FT   ACT_SITE    290    290       Proton donor.
FT   CARBOHYD     94     94       N-linked (GlcNAc. . .).
FT   CARBOHYD    220    220       N-linked (GlcNAc. . .).
FT   CARBOHYD    333    333       N-linked (GlcNAc. . .).
FT   DISULFID    161    372
FT   DISULFID    215    313
FT   DISULFID    347    351
FT   CONFLICT     15     24       SLGFLFLLFF -> AFASCFCFFC (in Ref. 5).
FT   CONFLICT     15     24       SLGFLFLLFF -> ALASCFCFFC (in Ref. 3 and
FT                                 4).
FT   CONFLICT     46     46       D -> H (in Ref. 5).
FT   CONFLICT     66     73       GFGQLTQL -> RIWPTHPA (in Ref. 4).
FT   CONFLICT     66     73       GFGQLTQL -> WIWPTHPA (in Ref. 4).
FT   CONFLICT     95     95       E -> D (in Ref. 3).
FT   CONFLICT    116    116       A -> R (in Ref. 3).
FT   CONFLICT    139    139       Q -> E (in Ref. 5).
FT   CONFLICT    157    157       P -> R (in Ref. 5).
FT   CONFLICT    212    212       P -> A (in Ref. 4).
FT   CONFLICT    215    215       C -> S (in Ref. 3).
FT   CONFLICT    294    294       S -> T (in Ref. 3).
FT   CONFLICT    372    372       C -> V (in Ref. 3).
FT   CONFLICT    383    383       D -> N (in Ref. 5).
FT   STRAND       34     43
FT   STRAND       47     47
FT   STRAND       50     50
FT   TURN         54     55
FT   STRAND       57     57
FT   HELIX        60     62
FT   STRAND       63     63
FT   TURN         64     65
FT   TURN         67     68
FT   STRAND       70     70
FT   HELIX        72     88
FT   TURN         89     93
```

Appendix 1 p.1

<!--StartFragment--> GenCore version 5.1.9

OM protein - protein search, using sw model

Run on: December 13, 2006, 18:30:08 ; Search time 196 Seconds
(without alignments)
898.104 Million cell updates/sec

Title: US-10-772-856-2
Perfect score: 2060
Sequence: 1 MGAVPLPLSPTASLSLGFLL.....DWATECMATSSHQGTVGALG 385

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2589679 seqs, 457216429 residues

Total number of hits satisfying chosen parameters: 2589679

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_8:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*
9: geneseqp2005s:*
10: geneseqp2006s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	2060	100.0	385	2	AAW30574	Aaw30574 Mouse pro
2	2006	97.4	381	8	ADQ89192	Adq89192 Mouse pro
3	1818	88.3	381	7	ADE57776	Ade57776 Rat Prote
4	1818	88.3	381	7	ADE64083	Ade64083 Rat Prote
5	1818	88.3	381	7	ADE57780	Ade57780 Rat Prote
6	1818	88.3	381	8	ADQ89194	Adq89194 Rat prost
7	1818	88.3	381	9	ADY37347	Ady37347 Rat prost
8	1818	88.3	381	9	AEC12592	Aec12592 Rat surro
9	1818	88.3	381	9	AEC12052	Aec12052 Rat surro
10	1661.5	80.7	386	2	AAW57418	Aaw57418 Protein e
11	1661.5	80.7	386	2	AAW95081	Aaw95081 Protein s
12	1661.5	80.7	386	3	AAY59293	Aay59293 Prostatic
13	1661.5	80.7	386	4	AAU06277	Aau06277 Prostatic
14	1661.5	80.7	386	4	AAB74820	Aab74820 Prostate
15	1661.5	80.7	386	4	AAU02172	Aau02172 Biomarker
16	1661.5	80.7	386	4	AAG62145	Aag62145 Human pro
17	1661.5	80.7	386	4	ABU71858	Abu71858 Human pro
18	1661.5	80.7	386	7	ADE57782	Ade57782 Human Pro
19	1661.5	80.7	386	7	ADE57778	Ade57778 Human Pro
20	1661.5	80.7	386	8	ADL66116	Adl66116 Human pro
21	1661.5	80.7	386	8	ADQ89193	Adq89193 Human pro
22	1661.5	80.7	386	8	ADR46064	Adr46064 Human pro
23	1661.5	80.7	386	9	ADY37348	Ady37348 Human pro
24	1661.5	80.7	386	9	AEC12373	Aec12373 Human sur
25	1661.5	80.7	386	9	AEC12739	Aec12739 Human sur
26	1661.5	80.7	386	9	AED95997	Aed95997 Human C-r
27	1661.5	80.7	515	2	AAW19762	Aaw19762 PAP-GM-CS

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28	1656.5	80.4	414	9	AED95999	Aed95999 Human C-r
29	1650.5	80.1	418	7	ADE64085	Ade64085 Human Pro
30	1605	77.9	585	4	ABU71889	Abu71889 Prostate
31	1605	77.9	585	6	ABR54580	Abr54580 Prostate
32	1605	77.9	585	7	ADB14470	Adb14470 FOPP/hPAP
33	1605	77.9	585	7	ADG26993	Adg26993 Human pro
34	1604	77.9	801	4	ABU71890	Abu71890 Prostate
35	1480	71.8	353	7	ADJ95104	Adj95104 Novel NOV
36	1480	71.8	353	7	ADJ95106	Adj95106 Novel NOV
37	1224.5	59.4	297	9	AED95998	Aed95998 Human C-r
38	1026.5	49.8	406	8	ADS10511	Ads10511 Human the
39	1022.5	49.6	423	5	AAO14067	Aao14067 Human lys
40	1022.5	49.6	423	7	ADE61363	Ade61363 Human Pro
41	1022.5	49.6	423	8	ABM81244	Abm81244 Tumour-as
42	1022.5	49.6	423	8	ADS88267	Ads88267 Human pro
43	1022.5	49.6	423	8	ADP23412	Adp23412 PRO polyp
44	1020.5	49.5	427	8	ADS11787	Ads11787 Human the
45	1019.5	49.5	423	7	ADE61361	Ade61361 Rat Prote

<!--EndFragment-->

Appendix 2, p 3

```
FT   STRAND       95     96
FT   HELIX        99    101
FT   STRAND      102    108
FT   HELIX       110    123
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FT   HELIX       128    130
FT   STRAND      132    132
FT   TURN        134    135
FT   STRAND      144    146
FT   HELIX       148    150
FT   STRAND      152    155
FT   STRAND      157    157
FT   STRAND      160    160
FT   HELIX       162    173
FT   HELIX       175    195
FT   STRAND      196    196
FT   STRAND      199    200
FT   HELIX       202    208
FT   TURN        209    209
FT   HELIX       210    218
FT   TURN        219    220
FT   TURN        225    226
FT   HELIX       229    247
FT   STRAND      248    251
FT   HELIX       252    258
FT   TURN        259    260
FT   HELIX       261    276
FT   STRAND      277    277
FT   TURN        278    279
FT   STRAND      282    288
FT   HELIX       290    299
FT   TURN        300    301
FT   STRAND      305    306
FT   TURN        310    311
FT   STRAND      313    321
FT   TURN        322    323
FT   STRAND      324    332
FT   TURN        335    336
FT   STRAND      337    337
FT   STRAND      340    341
FT   TURN        345    346
FT   STRAND      347    347
FT   STRAND      349    352
FT   HELIX       353    363
FT   STRAND      364    364
FT   STRAND      366    366
FT   HELIX       368    371
FT   TURN        372    372
SQ   SEQUENCE   386 AA;  44566 MW;  EF81E11DFAECADEA CRC64;

  Query Match             80.7%;  Score 1661.5;  DB 1;  Length 386;
  Best Local Similarity   81.6%;  Pred. No. 8e-120;
  Matches  311;  Conservative   28;  Mismatches   41;  Indels    1;  Gaps    1;

Qy          1 MGAVPLPLSPTASLSLGFLLLLSLCLDPG-QAKELKFVTLVFRHGDRGPIETFPTDPITE 59
              | | || |:  |||||||| ||   ||    ||||||||||||||| ||:||||||| |
Db          1 MRAAPLLLARAASLSLGFLFLLFFWLDRSVLAKELKFVTLVFRHGDRSPIDTFPTDPIKE 60

Qy         60 SSWPQGFGQLTQWGMEQHYELGSYIRKRYGRFLNDTYKHDQIYIRSTDVDRTLMSAMTNL 119
              |||||||||||| |||||||| |||||| :|||::|||:|:|||||||||||||||||
Db         61 SSWPQGFGQLTQLGMEQHYELGEYIRKRYRKFLNESYKHEQVYIRSTDVDRTLMSAMTNL 120

Qy        120 AALFPPEGISIWNPRLLWQPIPVHTVSLSEDRLLYLPFRDCPRFEELKSETLESEEFLKR 179
              ||||||||:||||| |||||||||| ||||:|||||||:||||:||:||||:|||| ||
Db        121 AALFPPEGVSIWNPILLWQPIPVHTVPLSEDQLLYLPFRNCPRFQELESETLKSEEFQKR 180

Qy        180 LHPYKSFLDTLSSLSGFDDQDLFGIWSKVYDPLFCESVHNFTLPSWATEDAMIKLKELSE 239
              ||||| |: ||  |||   ||||||||||||||:|||||||||||||||| | ||:||||
Db        181 LHPYKDFIATLGKLSGLHGQDLFGIWSKVYDPLYCESVHNFTLPSWATEDTMTKLRELSE 240

Qy        240 LSLLSLYGIHKQKEKSRLQGGVLVNEILKNMKLATQPQKYKKLVMYSAHDTTVSGLQMAL 299
              ||||||||||||||||||||||||||||| :|| |||   ||||:|||||||||||||||
Db        241 LSLLSLYGIHKQKEKSRLQGGVLVNEILNHMKRATQIPSYKKLIMYSAHDTTVSGLQMAL 300

Qy        300 DVYNGVLPPYASCHMMELYHDKGGHFVEMYYRNETQNEPYPLTLPGCTHSCPLEKFAELL 359
              |||||:|||||||||: ||| :|| :||||||||||||:||||| |||||: ||||||:||||:
```

```
Db        301 DVYNGLLPPYASCHLTELYFEKGEYFVEMYYRNETQHEPYPLMLPGCSPSCPLERFAELV 360

Qy        360 DPVIPQDWATECMATSSHQGT 380
              ||||||| |||| |:|||||
Db        361 GPVIPQDWSTECMTTNSHQGT 381
<!--EndFragment-->
```

Appendix 2 p.4

Appendix 3 p. 1

3 pages

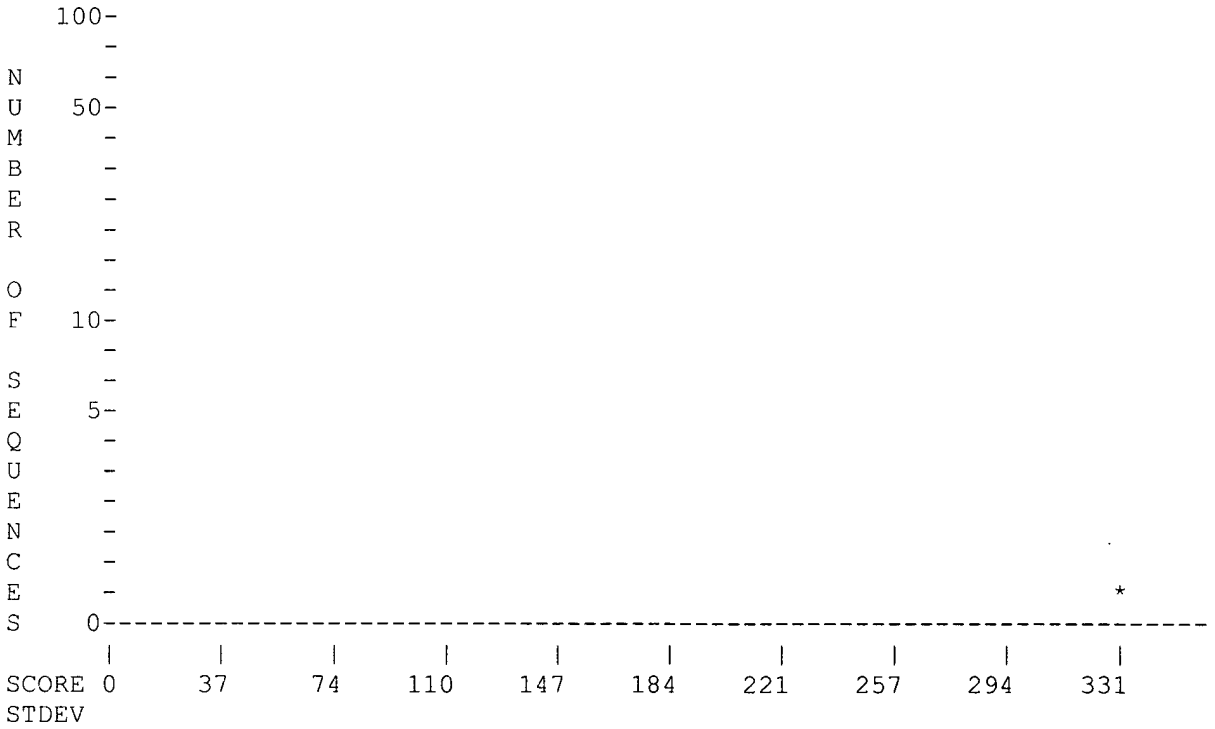
> O <
O| |O IntelliGenetics
> O <

FastDB - Fast Pairwise Comparison of Sequences
Release 5.4

Results file us-10-772-856-2.res made by tport on Thu 21 Dec 106 14:15:10-PST.

Query sequence being compared:US-10-772-856-2 (1-385)
Number of sequences searched: 1
Number of scores above cutoff: 1

Results of the initial comparison of US-10-772-856-2 (1-385) with:
File : 5882864.pep



PARAMETERS

Similarity matrix	PAM-150	K-tuple	1
Threshold level of sim.	16%		
Mismatch penalty	1	Joining penalty	20
Gap penalty	5.00	Window size	385
Gap size penalty	0.05		
Cutoff score	1		
Randomization group	0		

SEARCH STATISTICS

Scores:	Mean	Median	Standard Deviation
	331	0	0.00

Appendix 3 p 2

Times:	CPU	Total Elapsed
	00:00:00.00	00:00:00.00

Number of residues: 386
Number of sequences searched: 1
Number of scores above cutoff: 1

The scores below are sorted by initial score.
Significance is calculated based on initial score.

A 100% identical sequence to the query sequence was not found.

The list of best scores is:

PN5,882,864

Sequence Name	Description	Length	Init. Score	Opt. Score	Sig.	Frame
1. US-08-692-787-48	Sequence 48, Application	386	331	350	0.00	0

1. US-10-772-856-2 (1-385)
US-08-692-787-48 Sequence 48, Application US/08692787

Initial Score	=	331	Optimized Score	=	350	Significance =	0.00
Residue Identity	=	80%	Matches	=	311	Mismatches =	59
Gaps	=	1	Conservative Substitutions			=	15

```
X       10        20        30        40        50        60        70
MGAVPLPLSPTASLSLGFLLLLSLCLDPG-QAKELKFVTLVFRHGDRGPIETFPTDPITESSWPQGFGQLTQ
| | || |:  |||||||| ||    ||    ||||||||||||||||| ||:||||||| ||||||||||||
MRAAPLLLARAASLSLGFLFLLFFWLDRSVLAKELKFVTLVFRHGDRSPIDTFPTDPIKESSWPQGFGQLTQ
X       10        20        30        40        50        60        70

       80        90       100       110       120       130       140
WGMEQHYELGSYIRKRYGRFLNDTYKHDQIYIRSTDVDRTLMSAMTNLAALFPPEGISIWNPRLLWQPIPVH
 |||||||||  ||||||  :|||: |||:|:|||||||||||||||||||||||||:|||||  |||||||||
LGMEQHYELGEYIRKRYRKFLNESYKHEQVYIRSTDVDRTLMSAMTNLAALFPPEGVSIWNPILLWQPIPVH
      80        90       100       110       120       130       140

    150       160       170       180       190       200       210
TVSLSEDRLLYLPFRDCPRFEELKSETLESEEFLKRLHPYKSFLDTLSSLSGFDDQDLFGIWSKVYDPLFCE
||  ||||  |||||||  ||||  ||  ||||  ||||  |||||||  |  ||  |||   ||||||||||||||:||
TVPLSEDQLLYLPFRNCPRFQELESETLKSEEFQKRLHPYKDFIATLGKLSGLHGQDLFGIWSKVYDPLYCE
   150       160       170       180       190       200       210

  220       230       240       250       260       270       280
SVHNFTLPSWATEDAMIKLKELSELSLLSLYGIHKQKEKSRLQGGVLVNEILKNMKLATQPQKYKKLVMYSA
|||||||||||||  |  ||:|||||||||||||||||||||||||||||||||  ||  |||   ||||:||||
SVHNFTLPSWATEDTMTKLRELSELSLLSLYGIHKQKEKSRLQGGVLVNEILNHMKRATQIPSYKKLIMYSA
 220       230       240       250       260       270       280

290       300       310       320       330       340       350
HDTTVSGLQMALDVYNGVLPPYASCHMMELYHDKGGHFVEMYYRNETQNEPYPLTLPGCTHSCPLEKFAELL
||||||||||||||||  ||||||||: |||  :||  ||||||||||  |||||  ||||  |||||:||||
```

```
  HDTTVSGLQMALDVYNGLLPPYASCHLTELYFEKGEYFVEMYYRNETQHEPYPLMLPGCSPSCPLERFAELV
 290       300       310       320       330       340       350       360

360       370       380     X
  DPVIPQDWATECMATSSHQGTVGALG
   |||||||:|||| | |||||  :
  GPVIPQDWSTECMTTNSHQGTEDSTD
         370       380     X
```